



Mid-Season Influenza Vaccine Effectiveness Estimates for the 2013–2014 Influenza Season

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Mid-Season Influenza Vaccine Effectiveness Estimates for the 2013–2014 Influenza Season

Angelia A. Cost, PhD, ScM; Michelle J. Hiser, MPH; Zheng Hu, MS; Michael J. Cooper, PhD (CAPT, USPHS); Anthony W. Hawksworth; Jennifer M. Radin, MPH; Gary T. Brice, PhD (CDR, USN); Shauna C. Zorich, MD, MPH (Maj, USAF); Laurie S. DeMarcus, MPH; Katie J. Tastad, MPH; Jose L. Sanchez, MD, MPH (COL, USA, Ret)

The Department of Defense (DoD) conducts influenza surveillance for military members, dependents, and select civilian populations. The Armed Forces Health Surveillance Center (AFHSC), Naval Health Research Center (NHRC), and the U.S. Air Force School of Aerospace Medicine (USAFSAM) conduct annual mid-season influenza vaccine effectiveness (VE) analyses for the aforementioned populations. This report describes VE estimates at the midpoint for the 2013–2014 influenza season (29 September 2013 through 15 February 2014).

These three organizations performed separate analyses using the case-control method to estimate VE. Cases were individuals with positive laboratory tests for influenza during the first half of the 2013–2014 influenza season. In their individual studies, NHRC and USAFSAM used the control-test negative method for the selection of controls, while AFHSC used healthy controls.

AFHSC utilized data from the Defense Medical Surveillance System (DMSS) to identify all active component, non-recruit service members during the study period. Health Level 7 data in DMSS were used to identify influenza cases that were laboratory confirmed by a rapid influenza test, reverse transcriptase polymerase chain reaction (RT-PCR), or viral culture. Controls were active component service members with healthcare encounters for musculoskeletal conditions with no respiratory infections at the time of the encounters and no record of influenza during the study period. Controls were matched to cases by sex, age, date

of diagnosis (± 3 days), and treatment facility. Most cases and controls were treated at military or civilian medical facilities in the U.S.; however, the data did include service members who sought care at military treatment facilities (MTFs) in Europe, South Korea, Japan, and Guam. Vaccination status was determined by immunization records documented in DMSS.

The NHRC analysis relied on febrile respiratory illness (FRI) surveillance among DoD dependents living in Southern California and Illinois and civilians at clinics and hospitals near the U.S.–Mexico border from 25 November 2013 through 16 January 2014. Influenza cases were individuals who had positive laboratory tests for influenza by RT-PCR. Controls were FRI cases who tested negative for influenza. Vaccination status was determined by medical chart review. Individuals were considered vaccinated if their diagnoses occurred more than 14 days and less than 180 days since influenza vaccination.

The USAFSAM VE analyses were conducted using data generated from the DoD Global, Laboratory-based, Influenza Surveillance Program during the study period. Cases and controls were military dependents who presented to sentinel or other participating MTFs with influenza-like illness. As with AFHSC's analysis, most cases and controls presented to MTFs in the U.S.; however, dependents presenting to MTFs in Guam, Japan, and South Korea were also included. Cases were those who had positive laboratory tests for influenza by RT-PCR, viral culture, or multiplex PCR respiratory panel testing. Controls were

individuals who tested negative for influenza. Vaccination status was obtained from electronic immunization records or the program's surveillance questionnaire. Individuals were considered vaccinated if the vaccine was given at least 14 days prior to specimen collection.

Crude and adjusted odds ratios (ORs) were calculated using logistic regression. VE was defined as $(1 - \text{OR}) \times 100$.¹ When possible, analyses were stratified by influenza subtype and vaccine type (inactivated influenza vaccine [IIV] and live-attenuated influenza vaccine [LAIV]). Models were adjusted for 1) AFHSC: age, sex, and 5-year vaccination history for influenza as a dichotomous variable ($Y = \text{at least one vaccination in the previous 5 years}$, $N = \text{no vaccinations for influenza during the previous 5 years}$); 2) NHRC: age, hospitalization status (inpatient/outpatient), and surveillance population/location; and 3) USAFSAM: age group and time period (collapsed into four equal quartiles).

For the NHRC analyses of civilian and dependent populations, the estimated overall adjusted VE was 53% (95% confidence interval [CI], 17–74). By comparison, USAFSAM calculated an overall VE of 66% (95% CI, 51–76) for military dependents (Table). USAFSAM's subanalysis of VE by vaccine type (i.e., IIV and LAIV) indicated a statistically significant VE of 74% (95% CI, 60–83) for IIV and a statistically nonsignificant VE for LAIV (40%; 95% CI, -5–66). AFHSC's overall analyses estimated a nonsignificant VE for active component military members, 7% (95% CI, -32–35). Additional subanalyses by vaccine type also

TABLE. Mid-season influenza vaccine effectiveness (VE) among different populations for the 2013–2014 influenza season

Population	Viral subtype	Vaccine type	No. of cases (% vaccinated)	No. of controls (% vaccinated) ^a	Crude VE (95% CI)	Adjusted VE (95% CI) ^b
Active component service members (AFHSC)	Overall	Any type	518 (90)	2060 (91)	11 (-27–37)	7 (-32–35)
		IIV	183 (32)	1086 (48)	31 (0–53)	28 (-5–51)
		LAIV	324 (56)	910 (40)	-13 (-63–22)	-17 (-70–19)
Civilians and dependents (NHRC)	Overall	Any type	106 (19)	278 (33)	52 (17–72)	53 ^c (17–74)
	Influenza A (H1)	Any type	84 (17)	278 (33)	59 (23–78)	63 ^c (33–81)
Dependents (USAFSAM)	Overall	Any type	339 (26)	469 (39)	44 (24–59)	66 ^c (51–76)
		IIV	302 (17)	425 (33)	57 (38–70)	74 ^c (60–83)
		LAIV	234 (15)	248 (16)	6 (-54–42)	40 (-5–66)

^aAFHSC used healthy controls (matched to cases by sex, age, and date [+/- 3 days] and treatment facility) and NHRC and USAFSAM used unmatched influenza test negative controls.

^bAdjusted for 1) AFHSC: age, sex, 5-year prior vaccination status; 2) NHRC: age, hospitalization status (inpatient/outpatient) and surveillance population/location (overall VE only); or 3) USAFSAM: age group, time period (collapsed into four quartiles)

^cStatistically significant

Abbreviations: AFHSC=Armed Forces Health Surveillance Center; NHRC=Naval Health Research Center; USAFSAM=U.S. Air Force School of Aerospace Medicine; IIV=inactivated influenza vaccine; LAIV=live-attenuated influenza vaccine

produced nonsignificant estimates for VE (**Table**). Due to small sample sizes, NHRC was not able to compare VE by vaccine type or by influenza subtype.

Overall adjusted VE estimates for dependents and civilians included in these analyses indicated moderate protection and were similar to estimates published by other groups, including the Centers for Disease Control and Prevention (61%) and the Canadian Primary Care Sentinel Surveillance Network (74%).^{2,3} The civilian and dependent results suggest that the influenza vaccine reduced the risk of medically attended influenza from 53% to 66% among these populations. These findings demonstrate the benefits of the 2013–2014 seasonal influenza vaccine at mid-season.

These analyses indicate a statistically significant VE for the IIV vaccine in dependent and select civilian populations. VE was not statistically significant for LAIV. This finding is consistent with other published studies indicating IIV has a greater VE.^{4–8}

It has been suggested that the differences in effectiveness could be due to the inability of the live, attenuated viruses to stimulate antibody response due to recipients' past exposure to similar influenza viruses.^{8,9} LAIV has been shown to have a VE comparable to that of IIV in vaccine-naïve adult cohorts and similar or superior efficacy in infants and young children with limited histories of influenza vaccination.^{7,10–13}

VE estimations frequently differ between service members and civilians, with higher VE estimates seen among the latter. The most pronounced difference between these two groups is that influenza vaccination is mandatory for U.S. military members. This, in turn, leads to greater experience with, or exposure to, influenza vaccines, which might lead to a diminished antibody response and potentially diminished VE.^{14–17} In addition, the fact that the U.S. military starts vaccinating for influenza as early as August each year raises the possibility that individuals vaccinated

several months prior to the influenza season peak, typically in January or February, might be left unprotected due to waning immunity when the risk for infection is highest. Additional research aimed at understanding the impact of long vaccination histories (i.e., many vaccinations over many years) and regarding the duration of protection of influenza vaccines is needed to further elucidate these findings.

These analyses have limitations. The generalizability of these results is limited for various reasons. Cases were only included if the patients were sick enough to seek medical attention; therefore, we cannot comment on the vaccine's impact on less severe cases. Also, some vaccination data relied on patient recall and may not accurately reflect actual vaccination status. In addition, because the U.S. military population is younger and healthier than the general U.S. population, vaccine impact cannot be generalized to older, higher-risk populations. Lastly, estimation of VE by

specific influenza subtype and by type of vaccine (i.e., IIV and LAIV) could not be adequately examined given limitations of laboratory-based data and small numbers of infected individuals.

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